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10/544,207	08/17/2005	Thibaut Jose Wenzel	GRT/4662-46	8474

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EXAMINER	
WALICKA, MALGORZATA A	
ART UNIT	PAPER NUMBER
1652	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/544,207	WENZEL ET AL.	
	Examiner	Art Unit	
	MALGORZATA A. WALICKA	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *9,10 and 17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The amendment of Feb. 27, 2008 is acknowledged. Claims 1, 5 and 13-18 are amended; new claims 19-20 are added. Claims 1-8 and 11-16 belonging to the elected group I, are under examination.

Claims 9-10 and 17-20 are withdrawn from examiner's consideration as directed to a non-elected invention.

DETAILED ACTION

Restriction/election

Applicants request a rejoinder of nonelected method claims upon an indication that an elected product claim is allowable. This request is noted by the examiner.

Objections

Objections made in the Office action of Nov. 11, 2007 (previous action) are withdrawn, because of amendments.

Rejections

Rejections not repeated herein are withdrawn, because the claims are amended Applicants' arguments are persuasive.

35 USC 112 first paragraph

Written description

Claims 1-8 and 11-16 remain rejected under 35 U.S.C. 112, first paragraph.

The claims are directed to an oxalate deficient *A. niger* strain for production of any enzyme, wherein the enzyme production is at least the same as that produced by the wild type, as well as to the method of use of said strain for production of any enzyme/fungal amylase.

The claims are lacking sufficient written description of the claimed genus of oxalate deficient A. niger mutant strains, that produce a large and versatile genus of enzymes. The claimed mutated strain is characterized by

1) deficiency of oxalate production, and

2) at least the same production of an enzyme having any possible activity and being endogenous, exogenous, natively or recombinantly expressed in said mutated strain,

wherein the structure of the mutant is not sufficiently described. The disclosure teaches the UV mutants of A. niger CBS 513.88 that are oxalate deficient and naturally produce more amylase than their wild type (Table 5 and Fig. 7 of the disclosure). Applicants also teach an Aspergillus mutant called FINAl that has the oxlate dehydrogenase gene disrupted. The latter mutant when transfected with proline specific endoprotease and phospholipase A1genes expresses more of these enzymes than its transfected wild type. These mutants, UV mutants expressing in natural way more alpha amylase and FINAL mutant expressing recombinantly more proline specific endoprotease and phospholipase A1, do not identify the whole, astronomically large genus of mutants producing **any enzyme in the amount at least the same as in the**

wild type. In conclusion, one skilled in the art is not convinced that Applicants were in possession of the claimed invention at the time the application was filed.

Response to Applicants' traverse

Applicants on page 10 of REMARKS write,

A. "Applicants submit that their claimed invention relates to oxalate deficient A. niger strains that produce at least the same amount of a desired enzyme as the parent strain. Thus, two characterizing features of the claimed strains are:

(i) oxalate deficiency and

(ii) production of at least the same amount of the desired enzyme as the wild type strain produces under the same culture conditions."

Applicants argument has been fully considered, but is found not persuasive because although feature (i) of the mutant strain is taught by the disclosure, the term "the desired enzyme" is lacking a sufficient description of structure and function because amylase, proline specific endoprotease and phospholipase A1 do not identify any enzyme, and, in addition, the disclosure does not provide for their structure.

B. Furthermore, on the same page of Remarks Applicants point out,

"… there is no evidence that prior art A. niger mutant strains are suitable for production of enzyme in an industrial setting."

These arguments are not persuasive for the following reasons.

Regarding argument A, is found not persuasive because although feature (i) of the mutant strain is taught by the disclosure, the term "the desired enzyme" is lacking a sufficient description of its function and structure of the enzyme. Amylase, proline specific endoprotease and phospholipase A1 do not identify any enzyme, and, most importantly, the disclosure does not provide for the genetic structure of the mutant that determines production of any enzyme in at least the same amount as in the wild type. The structure of FINAL is known because it has oxalate hydrolase gene disrupted, however, as applicants found and art teaches, deficiency in oxalate level is not always related to the acitivity of oxalate hydrolase. The genetic structure of any of UV induced oxalate deficient mutants is not disclosed. Many different genetic structures of mutants can provide for oxalate deficiency and the functional characteristics of all ot them will be not the same. Disclosure of one mutant, FINAL, having a well identified genetic property, in no way leads a skilled artisan to other strains having similar properties. The disclosed mutant properties are not in fact identifying the necessary structure of Aspergillus niger mutants. In conclusion, Applicants do not teach that any enzyme, i.e. all enzymes, may be produced by any Aspargillus niger oxalate deficient mutant. structure.

Regarding argument B, it is related to rejection for anticipation by the prior art, however, the examiner wishes to point out that WO 00/50576 document used in the rejection under 35 USC 103 below refers to production of enzymes on the industrial scale. What is more important the instant claims do not comprise the limitation

"production of enzyme in an industrial setting". The argument is, therefore, not relevant to the rejection under this paragraph.

Scope of enablement

Claims 1-8 and 11-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for UV induced mutants oxalate deficient mutants of Aspergillus and an oxalate deficient Aspergillus strain FINALproducing1) native endogenous alpha amylase, and

2) exogenus proline endoproteinase, and

3) exogenous phospholipase A1;

does not reasonably enables any oxalate deficient Aspergillus strain, and method of use of said strain for production of any enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses

1) an extremely large genus of products that are all possible mutants of Aspergillus niger being oxalate deficient that naturally or in result of engineering produce at least the same amount of any enzyme as the wild type does;

2) use of 1) for production of said enzyme.

Although the art of production of Apergilus niger mutant being oxalate deficient is well known and skills of artisans high, to make and use the claimed invention requires from one skilled in the art research outside the realm of routine experimentation absent teaching function and the structure of the enzymes to be produced and the genetic structure of the mutants that assures said production. Firstly, the mutant must be tested for the oxalate level and the rest of the experimentation relates to testing levels of all possible enzymes in the mutant. Although the disclosure teaches explicitly production of three enzymes listed above, the teaching does not provide a guidance as to the structure of other oxalate deficient Aspergillus mutants wherein the structure enable production of any enzyme in at least the same level as in the wild type. Creating mutant FINAL does not provide such guidance. The broad scope of the claims covers the mutated strains for production of any, i.e. all enzymes, as long as their production is at least the same as that in the wild type. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the genetic structure of the Aspergillus mutant in which production on any enzyme is at least the same as in the wild type. Applicants do not provide such guidance by teaching two enzymes that are recombinantly produced in the mutant FINAL.

In summary, without a guidance on the part of Applicants in regards of the function and structure of the enzymes to be produced, experimentation left to those in the art is improperly extensive and undue.

35 USC 102

Claim 1 and 2 were rejected under 35 U.S.C. 102(b) as being anticipated by Pedersen et al. (Construction and Characterization of an Oxalic Acid Nonproducing Strain of *Aspergillus niger*, Metabolic Engineering, 2000, 2, 34-41). Claims 4-5, 7-8 and 11 were rejected under this paragraph as anticipated by WO 00/50576 published Aug. 31, 2000 .

Due to Applicants' arguments the rejection is withdrawn in the favor of rejection for obviousness as written below.

35 USC 103

Claims 1-2, 4-5, 6, 7 and 7-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/50576 published Aug. 31, 2000; included in the IDS, and further in the common knowledge of cell metabolism.

The claims are directed to an oxalate deficient Aspergillus niger mutant for production of any enzyme, wherein said enzyme is produced at at least the same amount as in the wild type and to a method of use of said mutant for production of said enzyme.

The document teaches that Apergilus niger is an organism wildly used for commercial production of industrial enzymes; passage bridging page 3 and 4, and

further teaches that production of oxalic acid by Aspergillus cell requires a lot of carbon, therefore expensive carbon sources must be added to the fermentation medium in comparison to what would be required only for production of the desired compound (page 2 line 5). WO document teaches Aspergillus *niger* strains mutated by physical or chemical agents including ultraviolet (page 19, lin 26) or by disrupting the *oha* gene (page 4 line 1 to start with) to have an oxalate deficient strain. Further, the WO document teaches oxalate deficient mutants transfected with homogenous or exogenous genes for production of many enzymes for large and small scale; see *Methods of Production* page 36-37 of the document. Among the enzymes listed by WO documents are amylolytic enzymes, lipolytic enzymes and proteolytic enzymes (page 23, line 3).

The WO document does not teach the level of the enzymes produced using the Aspergillus strain being deficient in oxalate production. One having skills in the art realizes that because the cellular metabolism includes thousands of enzymes, there will be in any mutated Aspergillus niger cell at least one enzyme that will be produced at the at least wild type level independently whether the enzyme is produced natively or recombinantly in said mutant cell.

It would have been therefore obvious for a person having ordinary skills in the art to use teachings of WO document and produce an oxalate deficient Aspergillus niger strain for the purpose of production of an enzyme, wherein production of an enzyme is at least the same as in the parental strain. Specifically, it would have been obvious to use UV for mutating the Aspergillus cell and it would have been obvious to make and

oxalate deficient cell having the oxalate dehydroganse gene disrupted.d. Furthermore, it would have been obvious to use said cell for production native amylase, recombiant proline endoproteinase and phospholipase A1, because these enzymes are form the genera of amylolytic, lipolytic and proteolytic enzymes suggested on page 23, line 3 of the WO document.

Altogether, the claimed invention would have been obvious because a person of ordinary skills had good reason to pursue the known options of using an oxalate deficient Aspergillus niger for production of an enzyme. The option was within the person technical grasp. This lead to an anticipate success of producing an enzyme at the at least the same level as in the wild type. Thus, the claimed product and its use is not of innovation but of ordinary skill and common sense.

In conclusion, the claimed invention was within the ordinary skill in the art to make and use at the time it was made, and was as a whole *prima facie* obvious.

Conclusion

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see

http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner

/Rebecca E. Prouty/
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